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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,513	12/13/2005	Nathalie Marie-Josephe Garcon	VB60298	6380

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EXAMINER
GRASER, JENNIFER E

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
01/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	10/560,513	GARCON ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35,37,39,41-48,51 and 53-59* is/are pending in the application.

4a) Of the above claim(s) *35,37,39,41-48,51 and 53-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-34 and for claims 19-21, 23-26, 29, 31-32 the Species DTPw (diphtheria toxoid, tetanus toxoid and inactivated whole-cell B.pertussis) and DTPa (diphtheria toxoid, tetanus toxoid and inactivated acellular B.pertussis), in the reply filed on 11/1/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 35 and 37, 39, 41-48, 51 and 53-59 are hereby withdrawn as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-4, 10, 11, 19, 23, 24, 26, 27, 29, 30 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Boehm et al (Pharm Res. Vol. 19. No. 9. Sept. 2002).

Boehm et al teach mono- and multivalent vaccines of *H.influenzae* type b (Hib)-TT conjugate, diphtheria toxoid (DT), tetanus toxoid (TT) and pertussis toxoid (PT) in poly (lactate) and poly(lactic-coglycolate) microspheres, e.g., a capsular polysaccharide of H.influenzae type B and a polyanionic polymer. The influence of coencapsulated

antigen and excipients on antigen loading, release and stability is examined. Strong and sustained antibody responses are elicited after single injection of tetravalent microsphere vaccines (DT + TT + PT + Hib) in guinea pigs. TT, DT, and PT were well known carrier proteins for the Hib polysaccharide which was known to not be very immunogenic on its own.

4. Claims 1-4, 10, 11, 19, 23, 24, 26, 27, 29, 30 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Gupta et al. "Gupta et al. Developments in Biological Standardization. Basel, CH, vol. 92. 1998, pages 63-78.

Gupta et al teaches that In recent years biodegradabte polymer microspheres have received much attention for the purposes of controlled release of antigens in order to reduce the number of doses needed for primary immunization to as few as a single dose and to target an antigen to microfold cells on mucosal surfaces after oral administration or to Ag-presenting cells after parenteral inoculations, A variety of vaccine antigens have been encapsulated in microspheres usually composed of poly (lactic/glycolic) acid (PLGA), Additionally, another adjuvant may be incorporated inside microspheres together with the Ag, further enhancing or modulating the immune response to the desired type, The major problem in developing controlled-release vaccines include instability of vaccine Ags during micro-encapsulation, storage and subsequent hydration. Tetanus toxoid (IT) and Haemophilus influenzae type b capsular polysaccharide conjugated to TT (Hib-T) is encapsulated inside PLGA microspheres and the Ab levels in mice are evaluated. A single injection of these micro-encapsulated vaccines elicited high Ab levels which persists for several months. The Ab levels are

similar or superior to those elicited by conventional formulations of AlPO4-adsorbed TT or soluble Hib-T conjugate vaccine.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 14-18 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta or Boehm as applied to claims 1-4, 10, 11, 19, 23, 24, 26, 27, 29, 30 and 33-34 above, and further in view of any one of Hilgers et al (WO 98/17310), Nicol et al (Gene Therapy, 9(20): 1351-1358, October 2002), Zhiqiang et al (J.Biomed. Materials Res. 6291), Oct. 2002, pp. 14-21, or Luka et al (International J. Radiation Oncology Bio. Physics, 55 (#), March 2003, pp. 707-712).

The teachings of Gupta and Boehm are set forth above. Although the Gupta and Boehm do not explicitly recite the concentrations of polyanionic polymers and amount of the Hib oligosaccharide/polysaccharide as recited in instant claims 14-18, these are result effective variables. The specific amount of adjuvant in the range of 100-1000 micrograms per 0.5mL dose as recited in instant claim 28 is a little bit higher than that disclosed in the primary references; however, it is in the same range. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the

optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. at 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since Applicant has not disclosed that the specific limitations recited in instant claims 14-18 are for any particular purpose or solve any stated problem and the prior art teaches that the concentration of the active ingredients and carriers of vaccines/immunogenic compositions often vary according to the subject being treated and the antigen which is being used, solutions and parameters appear to work equally as well, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the ingredients taught in the Gupta reference by normal optimization procedures known in the bacterial immunological arts.

6. Claims 5-9, 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta or Boehm as applied to claims 1-4, 10, 11, 14, 15, 16-19, 23, 24, 26, 27, 29, 30 and 33-34 above, and further in view of any one of Hilgers et al (WO 98/17310), Nicol et al (Gene Therapy, 9(20): 1351-1358, October 2002), Zhiqiang et al (J.Biomed. Materials Res. 6291), Oct. 2002, pp. 14-21, or Luka et al (International J. Radiation Oncology Bio. Physics, 55 (#), March 2003, pp. 707-712).

The teachings of Gupta and Boehm are set forth above. However, Gupta and Boehm do not specifically teach the use of different polyanionic polymers for microencapsulation (instant claims 5-9, 12 and 13).

The secondary references all teach the use of a variety of different polyanionic polymers for microencapsulation-sustained release formulations. Hilgers et al teach the use of a large variety of different polyanionic polymers as adjuvants for mucosal immunization with bacterial and/or viral antigens. See pages 4-8 of Hilgers et al which specifically teaches the same polyanionic polymers as recited in instant claism 5-9 and 12-13. It would have been prima facie obvious for one of ordinary skill in the art, absent evidence to the contrary, to use any one of these other polyanionic formulations in lieu of the poly (lactate) and poly(lactic-coglycolate), PLGA microspheres taught by Gupta and Boehm because the secondary references also teach the use of other polyanionic polymers for mucosal immunization and it appears that these other formulations would be expected to work equally as well as the ones taught by Boehm and Gupta.

7. Claims 20-22, 25, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta or Boehm as applied to claims 1-4, 10, 11, 14, 15, 16-19, 23, 24, 26, 27, 29, 30 and 33-34 above, and further in view of Boutriau et al (WO 02/00249)and Database Medsafe NEW ZEALAND MEDICINES AND MEDICAL DEVICES SAFETY AUTHORITY; 2002, GLAXOSMiTHKLINE NZ LTD: "Datasheet . Hiberix" XP002306401 retrieved from H1-1"P:/ANWW.MEDSAFE.GOV-r.NZJPROFS/DATASHEET /H/HIBERIXINJ, HTM..

The teachings of Gupta and Boehm are set forth above. However, Gupta and Boehm do not specifically teach the incorporation of one or more further antigens into the composition comprising the antigens specifically disclosed in instant claims 20-22, 25, and 31-32.

Boutriau et al teach a multivalent immunogenic composition comprising a conjugate of a carrier protein (tetanus toxoid, diphtheria toxoid, CRM197, protein D...) and the capsular polysaocharide of H. influenza type B, wherein said composition additionally comprise 2 or more further bacterial polysaccharides (e.g.N. meningitidis Y or W polysaccharide, Streptococcus pneumoniae 1...). One specific DTPw composition disclosed comprises: "TT, DT; Pw HepB (perferably adsorbed onto Al-phosphate), Hib (preferably conjugated onto "TT and/or unadsorbed), MenA (pref, conjugated onto protein-D) and MenO (pref conjugated onto protein D). Combination vaccines accordlng to Boutriau require substantially lower doses of Hib to obtain at least equivalent Ab titers. Boutriau mentions, that due to the known effect of carrier suppression, it is advantageous if in each of the compositions of the invention the polysaccharide Ag contained therein are conjugated to more than one carrier (p 3, lines 2-7, 23-33; p 5, 1ines 18-21; claims 12-15, 19, 20, 27-29).

Database Medsafe teaches that Hiberix (unabsorbed Hib-TT) can be mixed in the same syringe with SmithKline Beecham vaccine Infanrix (DTPa vaccine), Tritanrix (DTPw vaccine) or Tritanrix-HB (DTPw-HB vaccine).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent evidence to the contrary, that one or more further

antigens could be added into the compositions taught by Boehm or Gupta, specifically the antigens recited in instant claims 20-22, 25, and 31-32 because Boutriau and Database Medsafe specifically teach these type of combination vaccines with success. Boutriau specifically teaches one DTPw composition disclosed comprises: "TT, DT; Pw HepB (perferably adsorbed onto Al-phosphate), e.g., instant claims 31 and 32.

8. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15,1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Shanon Foley, can be reached on (571) 272-0898.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.

Jennifer Graser
Primary Examiner
Art Unit 1645

1/15/08